IN THE CLAIMS

Please cancel claims 2-4, 11, 14, 17, 19-21, 54-55, 64, 79, 86-87, 89-92, 94, 96-103, 105-107, 111-112, 119, 122, 127-129, 131-134, 136, 138-151, and 153-165.

I. Amendments to Pending Claims

Please substitute pending claims 1, 60, 104, 115, and 152 with the corresponding amended claims, as shown below.

1. (Currently Amended) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: ~~Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises:~~

(a) Providing a pharmaceutical composition in a topical hydroalcoholic gel dosage form, comprising:

i. testosterone;

ii. about 0.1% to about 5% (w/w) of at least one penetration enhancer selected from the group consisting of: isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, terpene, and combinations of any of the foregoing;

iii. about 30% to about 98% (w/w) of at least one alcohol; and

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iv. about 0.1% to about 5% (w/w) of at least one gelling agent;

wherein the dosage form is not a transdermal patch; and

(b) administering to the subject a pharmacologically effective amount of the gel to a selected area of skin such that upon once daily administration of the gel the testosterone is absorbed into the bloodstream of the subject at a rate and duration that maintains a steady-state circulating serum concentration of the testosterone that varies no more than 350 ng/dl during the approximate 24 hour period between each daily dose.

~~wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in at least one of the following:~~

~~(a) a serum testosterone C_{avg} of about 223 to about 797 ng/dL on the first day of administration to the subject;~~

~~(b) a serum testosterone C_{max} of about 288 to about 1178 ng/dL on the first day of administration to the subject;~~

~~(c) a serum testosterone C_{min} of about 92 to about 419 ng/dL on the first day of administration to the subject;~~

~~(d) a serum testosterone C_{avg} of about 304 to about 1086 ng/dL by the thirtieth consecutive day of administration to the subject;~~

~~(e) a serum testosterone C_{max} of about 410 to about 1682 ng/dL by the thirtieth consecutive day of administration to the subject;~~

~~(f) a serum testosterone C_{min} of about 212 to about 738 ng/dL by the thirtieth consecutive day of administration to the subject; or~~

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~~(g) a serum testosterone net $AUC_{(0-24)}$ of about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject~~.

2.-4. (Cancelled)

5. (Previously Amended) The method of claim 1, wherein the administration of the composition exhibits dose proportionality.

6. (Previously Amended) The method of claim 1, wherein the method results in a steady-state testosterone 24-hour pharmacokinetics profile in the male subject, wherein the profile exhibits a first testosterone serum concentration upon administration of the composition and exhibits a second testosterone serum concentration having a small increase compared to the first testosterone serum concentration at about two hours after application, followed by a decrease to a third testosterone serum concentration that remains relatively constant for the remainder of the day.

7. (Previously Amended) The method of claim 6, wherein the first testosterone serum concentration is between about 400 ng/dL to about 900 ng/dL, the second testosterone serum concentration is between about 500 ng/dL to about 1000 ng/dL , and the third testosterone serum concentration is between about 450 ng/dL to about 950 ng/dL.

8. (Previously Amended) The method of claim 6, wherein the third testosterone serum concentration is between about 300 ng/dL and about 1,000 ng/dL.

9. (Previously Amended) The method of claim 1, wherein the method causes an increased average dihydrotestosterone serum concentration in the male subject compared to the average dihydrotestosterone serum concentration of the male subject before administration of the composition.

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10. (Previously Amended) The method of claim 1, wherein the method causes an increase in the bone mineral density of the male subject compared to the bone mineral density of the male subject before administration of the composition.

11. (Cancelled)

12. (Previously Amended) The method of claim 1, wherein the method causes increased libido in the male subject compared to the libido of the male subject before administration of the composition.

13. (Previously Amended) The method of claim 1, wherein the method causes improved sexual performance in the male subject compared to the sexual performance of the male subject before administration of the composition.

14. (Cancelled)

15. (Previously Amended) The method of claim 1, wherein the method causes improved mood in the male subject compared to the mood of the male subject before administration of the composition.

16. (Previously Amended) The method of claim 1, wherein the method causes increased muscle strength in the male subject compared to the muscle strength of the male subject before administration of the composition.

17. (Cancelled)

18. (Previously Amended) The method of claim 1, wherein the method causes improved body composition in the male subject compared to the body composition of the male subject before administration of the composition.

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19.-21. (Cancelled)

27. (Previously Amended) The method of claim 1, wherein the testosterone comprises an enantiomer, a racemic mixture, a derivative, a base, or a salt thereof.

53. (Previously Amended) The method of claim 1, wherein the composition administered weighs about 1.0 gram to about 10 grams.

54.-55. (Cancelled)

57. (Previously Amended) The method of claim 1, wherein the composition comprises about 0.5 % to about 5 % testosterone.

58. (Previously Amended) The method of claim 1, wherein the composition comprises about 1 % testosterone.

60. (Currently Amended) The method of claim 1, wherein the penetration enhancer comprises ~~about 0.25 % to about 2.5 %~~ isopropyl myristate.

61. (Previously Amended) The method of claim 1, wherein the penetration enhancer comprises about 0.5 % isopropyl myristate.

62. (Previously Amended) The method of claim 1, wherein the gelling agent is polyacrylic acid.

63. (Previously Amended) The method of claim 62, wherein the composition comprises about 0.9 % polyacrylic acid.

64. (Cancelled)

79. (Cancelled)

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80. (Previously Added) The method of claim 1, wherein the serum testosterone concentration is maintained between about 400 ng testosterone per dl serum to about 1050 ng testosterone per dl serum.

81. (Previously Added) The method of claim 1, wherein for each about 0.1 gram per day administration of the composition to the skin, an increase of at least about 5 ng/dl in serum testosterone concentration results in the subject.

82. (Previously Added) The method of claim 1, wherein the composition is provided to the subject for daily administration in a dose of approximately 0.1 g, 2.5 g, 5 g, 7.5 g, or 10 g.

83. (Previously Added) The method of claim 82, wherein the dose is approximately a 5 g dose delivering about 50 mg to about 100 mg of testosterone to the skin.

84. (Previously Added) The method of claim 82, wherein the dose is approximately a 7.5 mg dose delivering about 50 mg to about 100 mg of testosterone to the skin.

85. (Previously Added) The method of claim 82, wherein the dose is approximately a 10 g dose delivering 50 mg to about 100 mg of testosterone to the skin.

86.-87. (Cancelled)

88. (Previously Added) The method of claim 1, wherein after at least about 30 days of daily administration serum testosterone concentration in the subject is at least about 490 ng/dl to about 860 ng/dl.

89.-92. (Cancelled)

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93. (Previously Added) Th method of claim 1, wherein the subject has primary hypogonadism prior to administration.

94. (Cancelled)

95. (Previously Added) The method of claim 1, wherein the subject has secondary hypogonadism prior to administration.

96.-103. (Cancelled)

104. (Currently Amended) A method of transdermally delivering testosterone to a male subject in need thereof, comprising:

(a) ~~preparing a hydroalcoholic gel composition which comprises~~ Providing a pharmaceutical composition in a topical hydroalcoholic gel dosage form, comprising:

i. testosterone;

ii. about 0.1% to about 5% (w/w) of at least one penetration enhancer selected from the group consisting of: isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, terpene, and combinations of any of the foregoing;

iii. about 30% to about 98% (w/w) of at least one alcohol ; and

iv. about 0.1% to about 5% (w/w) of at least one gelling agent;

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wherein the dosag form is not a transdermal patch; and

(b) administering to the subject a pharmacologically effective amount of the gel to a selected area of skin wherein for every about 0.1 g of gel/day administered, there is a corresponding increase of about 5 ng/dL in serum testosterone concentration.

~~(b) applying the composition to a selected area of skin of the subject in an amount effective to treat hypogonadism in the subject;~~

~~and wherein the composition does not comprise a glycol or a glycerol~~.

105.-107. (Cancelled)

108. (Previously Added) The method of claim 104, wherein the application of the composition exhibits dose proportionality.

109. (Previously Added) The method of claim 104, wherein the testosterone comprises an enantiomer, a racemic mixture, a derivative, a base, or a salt thereof.

110. (Previously Added) The method of claim 104, wherein the composition applied weighs about 1 gram to about 10 grams.

111.-112. (Cancelled)

113. (Previously Added) The method of claim 104, wherein the composition comprises about 0.5 % to about 5 % testosterone.

114. (Previously Added) The method of claim 104, wherein the composition comprises about 1% testosterone.

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115. (Currently Amended) The method of claim 104, wherein the penetration enhancer comprises ~~about 0.25% to about 2.5 %~~ isopropyl myristate.

116. (Previously Added) The method of claim 104, wherein the penetration enhancer comprises about 0.5% isopropyl myristate.

117. (Previously Added) The method of claim 104, wherein the gelling agent is polyacrylic acid.

118. (Previously Added) The method of claim 117, wherein the composition comprises about 0.9 % polyacrylic acid.

119. (Cancelled)

120. (Previously Added) The method of claim 104, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration that maintains a circulating serum concentration of the testosterone greater than about 400 ng testosterone per dl serum during a time period beginning about 2 hours after application and ending about 24 hours after application.

121. (Previously Added) The method of claim 104, wherein the serum testosterone concentration is maintained between about 400 ng testosterone per dl serum to about 1050 ng testosterone per dl serum during a time period beginning about 2 hours after application and ending about 24 hours after application.

122. (Cancelled)

123. (Previously Added) The method of claim 104, wherein the composition is provided to the subject for daily application in a dose of approximately 0.1 g, 2.5 g, 5 g, 7.5 g, or 10 g.

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124. (Previously Added) The method of claim 123, wherein the dose is approximately a 5 g dose delivering about 50 mg to about 100 mg of testosterone to the skin.

125. (Previously Added) The method of claim 123, wherein the dose is approximately a 7.5 mg dose delivering about 50 mg to about 100 mg of testosterone to the skin.

126. (Previously Added) The method of claim 123, wherein the dose is approximately a 10 g dose delivering 50 mg to about 100 mg of testosterone to the skin.

127.-129. (Cancelled)

130. (Previously Added) The method of claim 104, wherein after at least about 30 days of daily application serum testosterone concentration in the subject is about 490 ng/dl to about 860 ng/dl.

131.-134. (Cancelled)

135. (Previously Added) The method of claim 104, wherein the subject has primary hypogonadism prior to application.

136. (Cancelled)

137. (Previously Added) The method of claim 104, wherein the subject has secondary hypogonadism prior to application.

138.-151. (Cancelled)

152. (Currently Amended) A pharmaceutical composition in ~~the form of a hydroalcoholic~~ a topical hydroalcoholic gel dosage form, comprising:

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i. testosterone;

ii. about 0.1% to about 5% (w/w) of at least one penetration enhancer selected from the group consisting of: isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, terpene, and combinations of any of the foregoing; ~~and~~

iii. about 30% to about 98% (w/w) of at least one alcohol ; and

iv. about 0.1% to about 5% (w/w) of at least one gelling agent;

wherein the dosage form is not a transdermal patch; and

b. wherein when a pharmacologically effective amount of the gel is administered once daily to a selected area of skin of a male subject, the testosterone is absorbed into the bloodstream of the subject at a rate and duration that maintains a steady-state circulating serum concentration of the testosterone that varies no more than 350 ng/dl during the approximate 24 hour period between each daily dose.

~~wherein upon once daily administration of the composition to a selected area of skin of a subject, the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the administration results in at least one of the following:~~

~~(a) a serum testosterone C_{avg} of about 304 to about 1086 ng/dL by the thirtieth consecutive day of administration to the subject;~~

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~~(b) a serum testosterone C_{max} of about 410 to about 1682 ng/dL by the thirtieth consecutive day of administration to the subject;~~

~~(c) a serum testosterone C_{min} of about 212 to about 738 ng/dL on the thirtieth consecutive day of administration to the subject; or~~

~~(d) a serum testosterone net $AUC_{(0-24)}$ of about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject.~~

153.-165. (Cancelled)

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CONCLUSION

With entry of the above Supplemental Amendment B, it is respectfully submitted that the pending claims are in condition for allowance.

None of Applicants' amendments or cancellations are to be construed as dedicating any such subject matter to the public, and Applicants reserve all rights to pursue any such subject matter in this or a related patent application. The amendments are made solely to expedite prosecution.

The Examiner is invited to call Applicant's undersigned attorney at (312) 701-7283 for questions and to expedite prosecution.

Respectfully submitted,

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